

(FILE 'HOME' ENTERED AT 09:13:30 ON 05 AUG 2003)

FILE 'BIOSIS, MEDLINE, CAPLUS' ENTERED AT 09:13:56 ON 05 AUG 2003

L1	4 S IAP(10W)BIND? AND CELL CYCLE
L2	2 DUP REM L1 (2 DUPLICATES REMOVED)
L3	423 S IAP(10W)BIND?
L4	207 DUP REM L3 (216 DUPLICATES REMOVED)
L5	145 S IAP(10W)BIND? AND APOPTOSIS
L6	72 DUP REM L5 (73 DUPLICATES REMOVED)
L7	270 S SURVIVIN AND CELL CYCLE
L8	143 S SURVIVIN(15W)CELL CYCLE
L9	68 DUP REM L8 (75 DUPLICATES REMOVED)

=>

N 1999:26934 BIOSIS
 DN PREV199900026934
 TI IAP-family protein survivin inhibits caspase activity and **apoptosis** induced by Fas (CD95), bax, caspases, and anticancer drugs.
 AU Tamm, Ingo; Wang, Yan; Sausville, Ed; Scudiero, Dominic A.; Vigna, Nicole; Oltersdorf, Tilman; Reed, John C. (1)
 CS (1) Burnham Inst., 10901 North Torrey Pines Road, La Jolla, CA 92037 USA
 SO Cancer Research, (Dec. 1, 1998) Vol. 58, No. 23, pp. 5315-5320.
 ISSN: 0008-5472.
 DT Article
 LA English
 AB Survivin is a member of the inhibitor of **apoptosis** protein (IAP) family. We investigated the antiapoptotic mechanism of Survivin, as well as its expression in 60 human tumor cell lines used for the National Cancer Institute's anticancer drug screening program. In cotransfection experiments, cell death induced by Bax or Fas (CD 95) was partially inhibited (mean \pm SD, 65% \pm 8%) by Survivin, whereas XIAP, another IAP family member, almost completely blocked cell death (93% \pm 4%) under the same conditions. Survivin and XIAP also protected 293 cells from **apoptosis** induced by overexpression of procaspase-3 and -7 and inhibited the processing of these zymogens into active caspases. In vitro binding experiments indicated that, like other **IAP-family** proteins, survivin **binds** specifically to the terminal effector cell death proteases, caspase-3 and -7, but not to the proximal initiator protease caspase-8. Using a cell-free system in which cytosolic extracts were derived from control- or Survivin-transfected cells and where caspases were activated either by addition of cytochrome c and dATP or by adding recombinant active caspase-8, Survivin was able to substantially reduce caspase activity, cleavage of a tetrapeptide substrate, AspGluValAsp-aminofluorocoumarin. Similar results were obtained in intact cells when Survivin was overexpressed by gene transfection and caspase activation was induced by the anticancer drug etoposide. Survivin was expressed in all 60 cancer cell lines analyzed, with highest levels in breast and lung cancers and lowest levels in renal cancers. These findings indicate that Survivin, which is commonly expressed in human tumor cell lines, can bind the effector cell death proteases caspase-3 and -7 in vitro and inhibits caspase activity and cell death in cells exposed to diverse apoptotic stimuli. Although quantitative differences may exist, these observations suggest commonality in the mechanisms used by IAP-family proteins to suppress **apoptosis**.
 TI IAP-family protein survivin inhibits caspase activity and **apoptosis** induced by Fas (CD95), bax, caspases, and anticancer drugs.
 AB Survivin is a member of the inhibitor of **apoptosis** protein (IAP) family. We investigated the antiapoptotic mechanism of Survivin, as well as its expression in 60 human tumor cell. . . almost completely blocked cell death (93% \pm 4%) under the same conditions. Survivin and XIAP also protected 293 cells from **apoptosis** induced by overexpression of procaspase-3 and -7 and inhibited the processing of these zymogens into active caspases. In vitro binding experiments indicated that, like other **IAP-family** proteins, survivin **binds** specifically to the terminal effector cell death proteases, caspase-3 and -7, but not to the proximal initiator protease caspase-8. Using. . . apoptotic stimuli. Although quantitative differences may exist, these observations suggest commonality in the mechanisms used by IAP-family proteins to suppress **apoptosis**.
 IT Major Concepts

CUS (LOC): MMCASP3 GenBank (R)
 GenBank ACC. NO. (GBN): Y13086
 GenBank VERSION (VER): Y13086.1 GI:2094809
 CAS REGISTRY NO. (RN): 384754-53-4
 SEQUENCE LENGTH (SQL): 1297
 MOLECULE TYPE (CI): mRNA; linear
 DIVISION CODE (CI): Rodents
 DATE (DATE): 27 May 1997
 DEFINITION (DEF): M.musculus mRNA for **caspase-3**.
 SOURCE: house mouse.
 ORGANISM (ORGN): Mus musculus
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata;
 Euteleostomi; Mammalia; Eutheria; Rodentia;
 Sciurognathi; Muridae; Murinae; Mus
 NUCLEIC ACID COUNT (NA): 380 a 255 c 314 g 348 t
 REFERENCE: 1 (bases 1 to 1297)
 AUTHOR (AU): Van de Craen, M.; Vandenabeele, P.; Declercq, W.; Van den
 Brande, I.; Van Loo, G.; Molemans, F.; Schotte, P.; Van
 Criekinge, W.; Fiers, W.
 TITLE (TI): Characterization of seven murine caspase family members
 JOURNAL (SO): FEBS Lett., 403 (1), 61-69 (1997)
 OTHER SOURCE (OS): CA 126:235026
 REFERENCE: 2 (bases 1 to 1297)
 AUTHOR (AU): Van de Craen, M.
 TITLE (TI): Direct Submission
 JOURNAL (SO): Submitted (07-MAY-1997) M. Van de Craen, University of
 Gent, Laboratory of Molecular Biology, K.L.
 Ledeganckstraat 35, B-9000 Gent, BELGIUM

FEATURES (FEAT):

Feature Key	Location	Qualifier
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241 cactggaatg tcatctcgct ctggtacgga tgtggacgca gccaacctca gagagacatt
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L5 A

LOCUS (LOC): MMCASP7 GenBank (R)
 GenBank ACC. NO. (GBN): Y13088
 GenBank VERSION (VER): Y13088.1 GI:2094813
 CAS REGISTRY NO. (RN): 190306-99-1
 SEQUENCE LENGTH (SQL): 2372
 MOLECULE TYPE (CI): mRNA; linear
 DIVISION CODE (CI): Rodents
 DATE (DATE): 27 May 1997
 DEFINITION (DEF): M.musculus mRNA for **caspase-7**.
 SOURCE: house mouse.
 ORGANISM (ORGN): Mus musculus
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata;
 Euteleostomi; Mammalia; Eutheria; Rodentia;
 Sciurognathi; Muridae; Murinae; Mus
 NUCLEIC ACID COUNT (NA): 608 a 588 c 574 g 602 t
 REFERENCE: 1 (bases 1 to 2372)
 AUTHOR (AU): Van de Craen, M.; Vandenabeele, P.; Declercq, W.; Van den
 Brande, I.; Van Loo, G.; Molemans, F.; Schotte, P.; Van
 Criekinge, W.; Fiers, W.
 TITLE (TI): Characterization of seven murine caspase family members
 JOURNAL (SO): FEBS Lett., 403 (1), 61-69 (1997)
 OTHER SOURCE (OS): CA 126:235026
 REFERENCE: 2 (bases 1 to 2372)
 AUTHOR (AU): Van de Craen, M.
 TITLE (TI): Direct Submission
 JOURNAL (SO): Submitted (07-MAY-1997) M. Van de Craen, University of
 Gent, Laboratory of Molecular Biology, K.L.
 Ledeganckstraat 35, B-9000 Gent, BELGIUM

FEATURES (FEAT):

Feature Key	Location	Qualifier
source	1..2372	/organism="Mus musculus" /strain="C3H/An" /db-xref="taxon:10090" /cell-line="L929r2" /cell-type="fibrosarcoma"
CDS	190..1101	/standard-name="casp-7" /function="cysteine protease" /codon-start=1 /product="caspase-7" /protein-id="CAA73530.1" /db-xref="GI:2094814" /db-xref="SWISS-PROT:P97864" /translation="MTDDQDQAELEKVDSSSED GVDAKPDRSSIISILLKKKRNAS AGPVRTGRDRVPTYLYRMDFQKMGKCIINNKNF DKATGMDVRNGTDKDGALFKCFQ NLGFEVTVHNDSCAKMQDLLRKAEEDHSNSAC FACVLLSHGEEDLIYGKDGVTPIK DLTAHFRGDRCKTLLEKPKLFFIQACRGTELDDG IQADSGPINDIDANPRNKIPVEAD FLFAYSTVPGYYSWRNPGKGSWFVQALCSILNEH GKDLEIMQILTRVNDRVARHFESQ SDDPRFNEKKQIPCMVSMLTKELYFSR"

SEQUENCE (SEQ):

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L6 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1999:56316 CAPLUS
 DN 130:278037
 TI The **IAP family** of apoptotic regulators
 AU Eiben, Lisa J.; Duckett, Colin S.
 CS Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892-1578, USA
 SO Results and Problems in Cell Differentiation (1998), 24(Apoptosis: Mechanisms and Role in Disease), 91-104
 CODEN: RCLDAT; ISSN: 0080-1844
 PB Springer-Verlag
 DT Journal; General Review
 LA English
 AB A **review** with 54 refs. A perspective of the discovery and the evolution of our understanding of the inhibitor of **apoptosis** (IAP) proteins is presented. Structure and mechanism of action of vertebrate and invertebrate IAP proteins is discussed.
 RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT
 TI The **IAP family** of apoptotic regulators
 AB A **review** with 54 refs. A perspective of the discovery and the evolution of our understanding of the inhibitor of **apoptosis** (IAP) proteins is presented. Structure and mechanism of action of vertebrate and invertebrate IAP proteins is discussed.
 ST **review** IAP protein **apoptosis** regulation
 IT Proteins, specific or class
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (IAP (inhibitor of **apoptosis** protein); **IAP family** of apoptotic regulators)
 IT **Apoptosis**
 (IAP **family** of apoptotic regulators)

 L6 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1997:593613 CAPLUS
 DN 127:245874
 TI The iap genes: unique arbitrators of cell death
 AU Clem, Rollie J.; Duckett, Colin S.
 CS Dept of Molecular Microbiology and Immunology, The Johns Hopkins School of Hygiene and Public Health, Baltimore, MD, 21205, USA
 SO Trends in Cell Biology (1997), 7(9), 337-339
 CODEN: TCBIK; ISSN: 0962-8924
 PB Elsevier
 DT Journal; General Review
 LA English
 AB A **review** with 18 refs. The **iap family** of anti-apoptotic genes, originally discovered in viruses, has grown considerably in the past two years with the addn. of a no. of evolutionarily conserved cellular homologs. Although the mechanism(s) by which these novel proteins block cell death is still unknown, intriguing clues to their function have been revealed by the discovery of interactions between some of the IAP homologs and cellular proteins involved in carrying out apoptotic signaling. Here, Rollie Clem and Colin Duckett discuss how the various IAP proteins may function in regulating **apoptosis**.
 AB A **review** with 18 refs. The **iap family** of anti-apoptotic genes, originally discovered in viruses, has grown considerably in the past two years with the addn. of a no. of evolutionarily conserved cellular homologs. Although the mechanism(s) by which these novel proteins block cell death is still unknown, intriguing clues to their function have been revealed by the discovery of

interactions between some of the IAP homologs and cellular proteins involved in carrying out apoptotic signaling. Here, Rollie Clem and Colin Duckett discuss how the various IAP proteins may function in regulating **apoptosis**.

ST **review iap gene apoptosis**

IT Proteins, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(IAP (inhibitor of **apoptosis**); iap genes and IAP proteins in **apoptosis**)

IT **Apoptosis**

(iap genes and IAP proteins in **apoptosis**)

IT Gene, animal

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(iap; iap genes and IAP proteins in **apoptosis**)

=>

L9 ANSWER 68 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 DUPLICATE 40
 AN 1999:27863 BIOSIS
 DN PREV199900027863
 TI Control of apoptosis and mitotic spindle checkpoint by survivin.
 AU Li, Fengzhi; Ambrosini, Grazia; Chu, Emily Y.; Plescia, Janet; Tognin,
 Simona; Marchisio, Pier Carlo; Altieri, Dario C. (1)
 CS (1) Boyer Cent. Mol. Med., Dep. Pathol., Yale Univ. Sch. Med., 295
 Congress Ave., New Haven, CT 06536 USA
 SO Nature (London), (Dec. 10, 1998) Vol. 396, No. 6711, pp. 580-584.
 ISSN: 0028-0836.
 DT Article
 LA English
 AB Progression of the cell cycle and control of apoptosis (programmed cell
 death) are thought to be intimately linked processes, acting to preserve
 homeostasis and developmental morphogenesis. Although proteins that
 regulate apoptosis have been implicated in restraining cell-cycle entry
 and controlling ploidy (chromosome number), the effector molecules at the
 interface between cell proliferation and cell survival have remained
 elusive. Here we show that a new inhibitor of apoptosis (IAP) protein,
survivin, is expressed in the G2/M phase of the **cell**
cycle in a cycle-regulated manner. At the beginning of mitosis,
 survivin associates with microtubules of the mitotic spindle in a specific
 and saturable reaction that is regulated by microtubule dynamics.
 Disruption of survivin-microtubule interactions results in loss of
 survivin's anti-apoptosis function and increased caspase-3 activity, a
 mechanism involved in cell death, during mitosis. These results indicate
 that survivin may counteract a default induction of apoptosis in G2/M
 phase. The overexpression of survivin in cancer may overcome this
 apoptotic checkpoint and favour aberrant progression of transformed cells
 through mitosis.
 AB. . . between cell proliferation and cell survival have remained elusive.
 Here we show that a new inhibitor of apoptosis (IAP) protein,
survivin, is expressed in the G2/M phase of the **cell**
cycle in a cycle-regulated manner. At the beginning of mitosis,
 survivin associates with microtubules of the mitotic spindle in a
 specific. . .

=>

ANSWER 1 OF 251 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:206849 BIOSIS
DN PREV200300206849
TI Mammalian **IAP** gene **family**, primers, probes and
detection methods.
AU Korneluk, Robert G. (1); MacKenzie, Alexander E.; Baird, Stephen; Liston,
Peter
CS (1) Ottawa, Canada Canada
ASSIGNEE: Aegera Therapeutics Inc., Verdun, Canada
PI US 6541457 April 01, 2003
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Apr. 1 2003) Vol. 1269, No. 1, pp. No Pagination.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB Disclosed is substantially pure DNA encoding mammalian IAP polypeptides;
substantially pure polypeptides; and methods of using such DNA to express
the IAP polypeptides in cells and animals to inhibit **apoptosis**.
Also disclosed are conserved regions characteristic of the **IAP-**
family and primers and probes for the identification and isolation
of additional IAP genes. In addition, methods for treating diseases and
disorders involving **apoptosis** are provided.

L3 ANSWER 9 OF 251 CAPLUS COPYRIGH

N 1999:26934 BIOSIS

DN PREV199900026934

TI IAP-family protein survivin inhibits caspase activity and **apoptosis** induced by Fas (CD95), bax, caspases, and anticancer drugs.

AU Tamm, Ingo; Wang, Yan; Sausville, Ed; Scudiero, Dominic A.; Vigna, Nicole; Oltersdorf, Tilman; Reed, John C. (1)

CS (1) Burnham Inst., 10901 North Torrey Pines Road, La Jolla, CA 92037 USA

SO Cancer Research, (Dec. 1, 1998) Vol. 58, No. 23, pp. 5315-5320.

ISSN: 0008-5472.

DT Article

LA English

AB Survivin is a member of the inhibitor of **apoptosis** protein (IAP) family. We investigated the antiapoptotic mechanism of Survivin, as well as its expression in 60 human tumor cell lines used for the National Cancer Institute's anticancer drug screening program. In cotransfection experiments, cell death induced by Bax or Fas (CD 95) was partially inhibited (mean \pm SD, 65% \pm 8%) by Survivin, whereas XIAP, another IAP family member, almost completely blocked cell death (93% \pm 4%) under the same conditions. Survivin and XIAP also protected 293 cells from **apoptosis** induced by overexpression of procaspase-3 and -7 and inhibited the processing of these zymogens into active caspases. In vitro binding experiments indicated that, like other **IAP**-family proteins, survivin **binds** specifically to the terminal effector cell death proteases, caspase-3 and -7, but not to the proximal initiator protease caspase-8. Using a cell-free system in which cytosolic extracts were derived from control- or Survivin-transfected cells and where caspases were activated either by addition of cytochrome c and dATP or by adding recombinant active caspase-8, Survivin was able to substantially reduce caspase activity, cleavage of a tetrapeptide substrate, AspGluValAsp-aminofluorocoumarin. Similar results were obtained in intact cells when Survivin was overexpressed by gene transfection and caspase activation was induced by the anticancer drug etoposide. Survivin was expressed in all 60 cancer cell lines analyzed, with highest levels in breast and lung cancers and lowest levels in renal cancers. These findings indicate that Survivin, which is commonly expressed in human tumor cell lines, can bind the effector cell death proteases caspase-3 and -7 in vitro and inhibits caspase activity and cell death in cells exposed to diverse apoptotic stimuli. Although quantitative differences may exist, these observations suggest commonality in the mechanisms used by IAP-family proteins to suppress **apoptosis**.

TI IAP-family protein survivin inhibits caspase activity and **apoptosis** induced by Fas (CD95), bax, caspases, and anticancer drugs.

AB Survivin is a member of the inhibitor of **apoptosis** protein (IAP) family. We investigated the antiapoptotic mechanism of Survivin, as well as its expression in 60 human tumor cell. . . almost completely blocked cell death (93% \pm 4%) under the same conditions. Survivin and XIAP also protected 293 cells from **apoptosis** induced by overexpression of procaspase-3 and -7 and inhibited the processing of these zymogens into active caspases. In vitro binding experiments indicated that, like other **IAP**-family proteins, survivin **binds** specifically to the terminal effector cell death proteases, caspase-3 and -7, but not to the proximal initiator protease caspase-8. Using. . . apoptotic stimuli. Although quantitative differences may exist, these observations suggest commonality in the mechanisms used by IAP-family proteins to suppress **apoptosis**.

IT Major Concepts